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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/750,986	12/28/2000	Alexander Steinbuchel	Bayer 9998.2-HCL	1415

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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/750,986	STEINBUCHEL ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *3-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/976,063.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/28/00,5/8/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 1-13 are pending.

Applicant's preliminary amendment of claims 1-13, and election with traverse of Group IV, claims 1-2 drawn in part to a ferulic acid deacylase, in a communication filed on 6/1/2004 is acknowledged.

Applicant's traverse is on the ground(s) that the restriction should have been an election of species. Applicant's refer to an election of species applied to parent case 08/976063 by Examiner Peter Tung. Applicants submit that Examiner Tung's action was proper and shorter that the restriction requirement forwarded by the present Examiner. Applicants also submit that at the very least claims directed to making and use of ferulic acid deacylase should be examined on the merits. It is Applicant's contention that it is unclear as to why searching of multiple inventions would represent an undue burden to the Office.

Applicant's arguments have been fully considered but are not deemed persuasive to withdraw the restriction requirement. The Examiner acknowledges the election of species requested by Examiner Tung. It is noted however that the present Examiner determined that a restriction requirement was proper according to MPEP 806.04, 806.05, 808.01, 808.02 and 816. The Examiner clearly stated the reasons why the restriction was proper in paragraphs 2-6 and did not just merely state a conclusion. Furthermore, it is noted that the restriction requirement sent by the present Examiner is longer than that of Examiner Tung's in view of the fact that the Examiner is required to clearly explain the reasons why the restriction requirement is proper and also provide additional information which the Office considers to be useful for Applicants. In regard to arguments that searching multiple inventions would not impose an undue burden on the Office, it is noted that a comprehensive search of all groups would require not only a class/subclass search, but it will also require patented and non-patented literature searches which may not be co-

extensive. Therefore, a search of all inventions would impose an undue burden on the Office. In regard to arguments that claims directed to the making and use of ferulic acid deacylase should be included in the examination of the present application, it is noted that as indicated in paragraph 8-9 of the restriction requirement, process claims will be rejoined as long as the product claims are allowable and the process claims include all the limitations of the patentable product, in accordance with MPEP 821.04. Withdrawn process claims that are not commensurate in scope with an allowable product will not be rejoined. Since the product claims are not allowable, the Examiner is not required to rejoined method claims at the present time.

The requirement is deemed proper and therefore is made FINAL.

Claims 3-13 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

1. The specification is objected to as it lacks a Brief Description of the Drawings section. Appropriate correction is required.

Priority

2. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. 119(a)-(d) to GERMANY 19649655.1 filed on 11/29/1996. Certified copies of the foreign document have been received in application No. 08/976,063.

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 08/976,063 filed on 11/21/1997.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on 12/28/2000 and 5/8/2003 are acknowledged. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the Examiner.

Claim Objections

5. Claim 2 is objected to as the claim is still partially drawn to non-elected inventions. Examination of such claim will be restricted to the subject matter elected. For examination purposes, it will be assumed that claim 2 is directed to a ferulic acid deacylase. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 1-2 are indefinite in the recitation of "synthetic enzymes" as it is unclear if the term refers to enzymes which are associated with the synthesis of a compound or if the term refers to non-naturally occurring enzymes, i.e. enzymes not found in nature. It is noted that the specification does not provide a definition for the term either. For examination purposes, no patentable weight will be given to the term. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to a genus of enzymes which are associated with the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin or vanillic acid from eugenol. Claim 2 is directed to a genus of ferulic acid deacylases. See above for claim interpretation. While the specification discloses a Pseudomonas sp. HR 199 eugenol hydroxylase, a vanillin dehydrogenase, a coniferyl alcohol dehydrogenase, and a coniferylaldehyde dehydrogenase, the specification is completely silent in regard to a ferulic acid deacylase. There is no structure disclosed for a single ferulic acid deacylase nor there is any teaching as to how to isolate a ferulic acid deacylase. Furthermore, there is no disclosure of other enzymes from other organisms which are associated with the conversion of eugenol to coniferyl alcohol, coniferylaldehyde, ferulic acid vanillin or vanillin acid. No information has been presented regarding a correlation between structure and the enzymatic activity desired.

The genus of polypeptides claimed is a large, structurally variable genus. While a sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus., in the instant case, there is no structural feature which is representative of all the members of the genus of enzymes recited in the claims. While the argument can be made that a genus of polypeptides is adequately described by the structures disclosed in the specification since one could apply structural homology to isolate polypeptides of similar function, it is noted that the art teaches that even homologs sharing high structural similarity, may not share similar function. Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one

amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Therefore, in the absence of any additional information correlating structure with the desired enzymatic function, or any correlation between the structures disclosed in the specification and enzymatic activity, many structurally unrelated polypeptides are encompassed by the genus. The specification fails to disclose a single ferulic acid deacylase and only discloses a single eugenol hydroxylase, a vanillin dehydrogenase, a coniferyl alcohol dehydrogenase, and a coniferylaldehyde dehydrogenase, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the genus of polypeptides claimed. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed.

11. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 2 is directed to any ferulic acid deacylase. The specification, while indicating that one of the embodiments of the invention is a ferulic acid deacylase, fails to disclose a single ferulic acid deacylase. No structure of a ferulic acid deacylase has been provided nor there is any teaching as to how one of skill in the art can isolate a ferulic acid deacylase. There are no working examples and no correlation between structure and ferulic acid deacylase activity has been provided such that one of skill

in the art could determine whether a polypeptide having specific structural elements also has ferulic acid deacylase activity. Therefore, due to the complete lack of information as to how the structure of a ferulic acid deacylase or how one of skill in the art can obtain a ferulic acid deacylase, the lack of knowledge as to the structural elements required in any polypeptide to display ferulic acid deacylase activity, and the lack of working examples, one of skill in the art cannot reasonably conclude that the specification provides any guidance to enable one of skill in the art to make and use the claimed invention.

12. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a single Pseudomonas sp. HR 199 eugenol hydroxylase, vanillin dehydrogenase, coniferyl alcohol dehydrogenase, and coniferylaldehyde dehydrogenase, does not reasonably provide enablement for (1) any enzyme associated with the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin or vanillin acid from eugenol, or (2) any eugenol hydroxylase, vanillin dehydrogenase, coniferyl alcohol dehydrogenase, or coniferylaldehyde dehydrogenase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claim, as described above, is not commensurate with the enablement provided in regard to the extremely large number of unknown enzymes encompassed by the claim. As indicated above, while the specification discloses a single Pseudomonas sp. HR 199 eugenol hydroxylase, a vanillin dehydrogenase, a coniferyl alcohol dehydrogenase, and a coniferylaldehyde dehydrogenase, the

specification is completely silent in regard to other enzymes from other organisms which are associated with the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin or vanillin acid from eugenol. No disclosure of the critical structural elements required in any polypeptide to display the desired enzymatic activity has been presented. Also, there is no disclosure of the structural elements in the enzymes disclosed which are associated with the desired activity. Furthermore, the specification provides no clue as to the structure of a single ferulic acid deacylase nor does it provide any teaching as to how one of skill in the art can isolate a ferulic acid deacylase. While the argument can be made that other enzymes with the desired activity can be obtained using structural homology, it is reiterated herein that the art, as evidenced by Witkowski et al., Broun et al. and Seffernick et al. discussed above, teaches the unpredictability of assigning function based solely on structural homology. Since structure determines function, one of skill in the art would require some knowledge or guidance as to which are the structural elements required in a polypeptide to display the desired activity. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to display the desired function, and the unpredictability of the prior art in regard to function based on structural homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate the claimed enzymes. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Priefert et al. (J. Bacteriol 179(8):2595-2607, April 1997). Claim 1 is directed in part to an enzyme which is associated with the conversion of eugenol to vanillic acid. The production of vanillic acid from eugenol requires the conversion of vanillin to vanillic acid. Priefert et al. teaches a Pseudomonas vanillin dehydrogenase (vdh), which catalyzes the conversion of vanillin to vanillic acid (Abstract; Figure 1, Figure 4). Therefore, the teachings of Priefert et al. anticipate claim 1 as written.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Jaeger et al. (Current Microbiology 6:333-336, 1981). Claim 1 is directed in part to an enzyme which is associated with the conversion of eugenol to coniferylaldehyde. The production of coniferylaldehyde from eugenol requires the conversion of coniferyl alcohol to coniferylaldehyde. Jaeger et al. teaches the isolation and purification of a Rhodococcus erythropolis coniferyl alcohol dehydrogenase (Abstract; page 334, Purification of the enzyme). Therefore, the teachings of Jaeger et al. anticipate claim 1 as written.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6524831. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 1 of U.S. Patent No. 6524831 is directed to a eugenol hydroxylase comprising two subunits encoded by polynucleotides comprising SEQ ID NO: 11 and SEQ ID NO: 15. Claim 1 of the instant application is directed in part to an enzyme associated in the production of coniferyl alcohol from eugenol. Therefore, claim 1 of U.S. Patent No. 6524831 anticipates the instant claim as written.

Conclusion

17. No claim is in condition for allowance.

18. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

19. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through

Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
June 18, 2004

REBECCA E. PRUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600